



# Proteomic profiling and its applications to muscle aging and sarcopenia

Ali Mobasher<sup>\*</sup>

Musculoskeletal Research Group, Division of Veterinary Medicine, Faculty of Medicine and Health Sciences, School of Veterinary Medicine and Science, University of Nottingham, Nottingham, UK

<sup>\*</sup>Correspondence: [ali.mobasher@nottingham.ac.uk](mailto:ali.mobasher@nottingham.ac.uk)

## A commentary on

### Proteomic profiling of fast-to-slow muscle transitions during aging

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Aging causes dramatic changes in the musculoskeletal system. Muscle, bone, cartilage, and tendon are all affected. For example, bone mass is reduced as people age, especially in women after menopause. The bones become lighter and less dense as they lose calcium and other minerals. Intervertebral disks lose fluid and become thinner, compromising their gel-like properties and their ability to withstand load. Synovial joints become stiff and lose their flexibility. Articular cartilage becomes drier, thinner, and much more fragile and synovial fluid loses some of its lubricating properties. This eventually results in the erosion of cartilage, formation of osteophytes, and changes in subchondral bone.

Sarcopenia is the degenerative loss of skeletal muscle structure and function associated with the aging process. Age-related changes in muscle mass, structure, and function can be particularly dramatic. The gradual loss of muscle tissue (atrophy) reduces total body mass. The age-related alterations in muscle involve age-related muscle fiber transitions and metabolic shifts in aging muscle. These alterations collectively affect posture and gait and these changes are particularly evident in our seventies, eighties, and nineties. These changes involve anatomical, morphological, and enzymatic alterations in muscle (Grimby et al., 1982). In older individuals the normal physiological turnover of muscle is compromised and older muscle is replaced much more slowly, and the lost muscle may be replaced with adipose tissue or a tough fibrous connective tissue. The deposition of lipofuscin (also known as the aging pigment and by-product of lysosomal degrada-

tion) and lipids in muscle affects function and there a change in relative muscle fiber composition with age where muscle fibers effectively shrink (Grimby et al., 1984). These changes in muscle, combined with normal aging changes in the nervous system, reduce muscular tone and contraction. Muscles become rigid like joints and do not recover their tone, even with regular physical exercise. Aging is therefore a complex process but in muscle it is usually associated with a decrease in mass, strength, and efficiency of contraction. However, in essence, there is a generalized decline in muscle protein synthesis (Grimby and Saltin, 1983). The underlying mechanism of functional changes in aging muscle has yet to be fully understood.

“Physiology and Pathophysiology of Musculoskeletal Aging” is a Frontiers Research Topic aimed at increasing our understanding of musculoskeletal aging, placing special emphasis on healthy aging as a key research priority. Proteomics and mass spectrometry have been successfully applied to crude extracts and subcellular fractions of skeletal muscle to identify novel aging marker proteins in animal models of aging and human muscle tissues from elderly subjects. In this Research Topic Kay Ohlendieck reviews the applications of proteomic profiling to aging muscle and the “fast-to-slow” muscle transitions that are thought to occur during aging. The author discusses proteomic profiling approaches that have helped to establish an age-related shift to slower protein isoforms of myosin heavy chain, myosin light chain, actin, and tropomyosin (TM), as well as subunits of troponin (Ohlendieck, 2011). His mini-review also discusses the “glycolytic-to-oxidative” shift that occurs in slower-twitching senescent muscles and the newly identified proteins that are altered in aging muscle using proteomic profiling (Ohlendieck, 2011). Proteomic profiling has also revealed an increase in mitochon-

drial enzymes and concomitant decrease in glycolytic enzymes during the fast-to-slow transformation process in aging skeletal muscle. This timely mini-review also discusses alterations in metabolic and contractile elements that can be used to define a “sarcopenia-specific” biomarker signature.

The preservation of skeletal muscle mass is central to maintaining mobility and quality of life with aging and also impacts on our capacity to recover from illness and injury (Murton and Greenhaff, 2010). Muscle mass loss accompanies periods of bedrest and limb immobilization in humans (Marimuthu et al., 2011). This is something that elderly human patients may frequently experience especially if they undergo major operations and are hospitalized for other age-related diseases. Studies investigating processes underlying disuse-induced muscle atrophy provide us with an opportunity to study temporal changes in cellular and molecular processes in muscle (Murton and Greenhaff, 2010). Proteomic profiling has many potential applications in this area. This area of research raises some important questions and paves the way forward for future areas of investigation. A substantial body of evidence has accumulated over the past 35 years in support of a role for reactive oxygen species (ROS) oxidative damage to the mitochondrial respiratory chain and mitochondrial DNA in aging (Jang and Remmen, 2009). More studies are clearly required to fully understand the role of mitochondria in age related disease and aging. These mitochondrial changes are thought to contribute to sarcopenia and muscle aging (Fulle et al., 2004). This article gives hope to muscle researchers who have adopted (or are planning to employ) proteomic profiling as tool for exploring the bioenergetic changes that occur in aging muscle and the determining potential relevance of the mitochondrial theory of aging to sarcopenia. This approach may also be useful for studies aimed at unrave-

ling the role of satellite cells and innervation in skeletal repair and adaptation and the potential for reversing skeletal muscle atrophy (Carlson, 1995), especially in the context of ROS imbalance induced by an increased oxidative metabolism (Celegato et al., 2006). Clearly there is a need for more dialog and discussion between researchers in closely related fields (e.g., endocrinology, skeletal muscle, physiology, exercise physiology, gerontology) and for multidisciplinary approaches in order to gain greater insight into sarcopenia. This is one of the overarching objectives of this Frontiers Research Topic.

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